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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
NEWS 3	AUG 18	COMPENDEX indexing changed for the Corporate Source (CS) field
NEWS 4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS 5	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents
NEWS 6	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS 7	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus
NEWS 8	OCT 21	Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded
NEWS 9	OCT 21	Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models
NEWS 10	NOV 23	Addition of SCAN format to selected STN databases
NEWS 11	NOV 23	Annual Reload of IFI Databases
NEWS 12	DEC 01	FRFULL Content and Search Enhancements
NEWS 13	DEC 01	DGENE, USGENE, and PCTGEN: new percent identity feature for sorting BLAST answer sets
NEWS 14	DEC 02	Derwent World Patent Index: Japanese FI-TERM thesaurus added
NEWS 15	DEC 02	PCTGEN enhanced with patent family and legal status display data from INPADOCDB
NEWS 16	DEC 02	USGENE: Enhanced coverage of bibliographic and sequence information
NEWS 17	DEC 21	New Indicator Identifies Multiple Basic Patent Records Containing Equivalent Chemical Indexing in CA/CAplus

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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FILE 'HOME' ENTERED AT 14:01:42 ON 31 DEC 2009

=> caplus
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The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.44       0.44

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FILE COVERS 1907 - 31 Dec 2009  VOL 152 ISS 1
FILE LAST UPDATED: 30 Dec 2009  (20091230/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Oct 2009

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

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E2            4     US2002/BI
E3            0 --> US2002-060759/BI
E4            1     US2002183683/BI
E5            2     US20030000388213/BI
E6            1     US20030059376A1/BI
E7            1     US20030156532A1/BI
E8            1     US20030202444A1/BI
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E12           1     US2004006506 7A1/BI
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E11           1     US2002-60769/AP
E12           1     US2002-60776/AP

=> s e3
L1            1 US2002-60759/AP

=> d ll 1 ibib ind

L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2000:209821  CAPLUS
DOCUMENT NUMBER:          132:217135
TITLE:                    Treatment of chronic lymphocytic leukemia
INVENTOR(S):              Lerner, Adam
PATENT ASSIGNEE(S):       Boston Medical Center Corp., USA
SOURCE:                   PCT Int. Appl., 44 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     --------------      ----   --------    -------------------      --------
     WO 2000016621        A1    20000330    WO 1999-US21518          19990917
         W:  AU, CA, JP, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     AU 9960470           A     20000410    AU 1999-60470            19990917
     US 6399649           B1    20020604    US 2000-423349           20000501
     US 20030018014       A1    20030123    US 2002-60759            20020130 <--
PRIORITY APPLN. INFO.:                      US 1998-101721P     P    19980924
                                            WO 1999-US21518     W    19990917
                                            US 2000-423349      A3   20000501
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
IC   ICM  A01N037-18
     ICS  A61K038-00
CC   1-6 (Pharmacology)
ST   chronic lymphocytic leukemia treatment cyclic adenosine monophosphate
     phosphodiesterase inhibitor
IT   Antitumor agents
        (chronic lymphocytic leukemia treatment by type 4 cyclic adenosine
        monophosphate phosphodiesterase inhibitors)
IT   Leukemia
        (chronic lymphocytic; chronic lymphocytic leukemia treatment by type 4
        cyclic adenosine monophosphate phosphodiesterase inhibitors)
IT   61413-54-5, Rolipram
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (chronic lymphocytic leukemia treatment by)
IT   9036-21-9, Cyclic adenosine monophosphate phosphodiesterase
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (type 4, inhibitors; chronic lymphocytic leukemia treatment by)
```

```
OS.CITING REF COUNT:      3     THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
                                (3 CITINGS)
REFERENCE COUNT:          1     THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> file zcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     5.50       5.94

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FILE COVERS 1907 - 31 Dec 2009  VOL 152 ISS 1
FILE LAST UPDATED: 30 Dec 2009  (20091230/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Oct 2009
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=> set expand continuous
SET COMMAND COMPLETED

=> e  Cyclic adenosine monophosphate phosphodiesterase inhibitor/ct
E#   FREQUENCY     AT     TERM
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E13          0     11     CYCLIC 3',5'-NUCLEOTIDE PHOSPHODIESTERASE/CT
E14          0      2     CYCLIC ACETALS/CT
E15          0        --> CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE INHIB
                          ITOR/CT
E16          0     26     CYCLIC ADP-RIBOSE/CT
E17          0      2     CYCLIC ADP-RIBOSE HYDROLASE 2/CT
E18          0      2     CYCLIC ADP-RIBOSE SYNTHETASE/CT
E19          0      2     CYCLIC ALCOHOLS/CT
E20          0      2     CYCLIC ALIPH. EPOXY RESINS/CT
E21          0      2     CYCLIC ALKANES/CT
E22          0      3     CYCLIC ALKENEDIYNES/CT
E23          0      2     CYCLIC ALKENES/CT
E24          0      3     CYCLIC ALKYNES/CT
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=> e  Cyclic adenosine monophosphate phosphodiesterase/ct
E#   FREQUENCY     AT      TERM
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E25          0     11      CYCLIC 3',5'-NUCLEOTIDE PHOSPHODIESTERASE/CT
E26          0      2      CYCLIC ACETALS/CT
E27          0        --> CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE/CT
E28          0     26      CYCLIC ADP-RIBOSE/CT
E29          0      2      CYCLIC ADP-RIBOSE HYDROLASE 2/CT
E30          0      2      CYCLIC ADP-RIBOSE SYNTHETASE/CT
E31          0      2      CYCLIC ALCOHOLS/CT
E32          0      2      CYCLIC ALIPH. EPOXY RESINS/CT
E33          0      2      CYCLIC ALKANES/CT
E34          0      3      CYCLIC ALKENEDIYNES/CT
E35          0      2      CYCLIC ALKENES/CT
E36          0      3      CYCLIC ALKYNES/CT

=> e  phosphodiesterase inhibitor/ct
E#   FREQUENCY     AT      TERM
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E37          0     14      PHOSPHODIESTERASE II/CT
E38          0      2      PHOSPHODIESTERASE III/CT
E39          0        --> PHOSPHODIESTERASE INHIBITOR/CT
E40          0      2      PHOSPHODIESTERASE V/CT
E41          0      2      PHOSPHODIESTERASE, ADENOSINE CYCLIC 3',5'-PHOSPHATE/CT
E42          0      2      PHOSPHODIESTERASE, CYCLIC 2',3'-NUCLEOTIDE 3'-/CT
E43          0      2      PHOSPHODIESTERASE, CYCLIC 3',5'-NUCLEOTIDE/CT
E44          0      2      PHOSPHODIESTERASE, CYCLIC NUCLEOTIDE/CT
E45          0      2      PHOSPHODIESTERASE, GUANOSINE CYCLIC 3',5'-PHOSPHATE/CT
E46          0      1      PHOSPHODIESTERASE-INHIBITING/CT
E47          0      2      PHOSPHODIESTERASE-INHIBITING MOLECULAR STRUCTURE-BIOLO
                           GICAL ACTIVITY RELATIONSHIP/CT
E48          0      2      PHOSPHODIESTERASE-IV/CT

=> e e46
E#   FREQUENCY     AT      TERM
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E49          0      2      PHOSPHODIESTERASE, CYCLIC NUCLEOTIDE/CT
E50          0      2      PHOSPHODIESTERASE, GUANOSINE CYCLIC 3',5'-PHOSPHATE/CT
E51          0      1 --> PHOSPHODIESTERASE-INHIBITING/CT
E52          0      2      PHOSPHODIESTERASE-INHIBITING MOLECULAR STRUCTURE-BIOLO
                           GICAL ACTIVITY RELATIONSHIP/CT
E53          0      2      PHOSPHODIESTERASE-IV/CT
E54          0      2      PHOSPHODIESTERS/CT
E55          3             PHOSPHODOXINS/CT
E56          0      1      PHOSPHOENOLPYRUVATE/CT
E57          0     21      PHOSPHOENOLPYRUVATE CARBOXYKINASE/CT
E58          0     22      PHOSPHOENOLPYRUVATE CARBOXYKINASE (ATP)/CT
E59          0      2      PHOSPHOENOLPYRUVATE CARBOXYKINASE (EC 4.1.1.49)/CT
E60          0     12      PHOSPHOENOLPYRUVATE CARBOXYKINASE (GUANOSINE TRIPHOSPH
                           ATE)/CT

=> e  phosphodiesterase IV/ct
E#   FREQUENCY     AT      TERM
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E61          0     14      PHOSPHODIESTERASE II/CT
E62          0      2      PHOSPHODIESTERASE III/CT
E63          0        --> PHOSPHODIESTERASE IV/CT
E64          0      2      PHOSPHODIESTERASE V/CT
E65          0      2      PHOSPHODIESTERASE, ADENOSINE CYCLIC 3',5'-PHOSPHATE/CT
E66          0      2      PHOSPHODIESTERASE, CYCLIC 2',3'-NUCLEOTIDE 3'-/CT
E67          0      2      PHOSPHODIESTERASE, CYCLIC 3',5'-NUCLEOTIDE/CT
E68          0      2      PHOSPHODIESTERASE, CYCLIC NUCLEOTIDE/CT
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E69           0     2     PHOSPHODIESTERASE, GUANOSINE CYCLIC 3',5'-PHOSPHATE/CT
E70           0     1     PHOSPHODIESTERASE-INHIBITING/CT
E71           0     2     PHOSPHODIESTERASE-INHIBITING MOLECULAR STRUCTURE-BIOLO
                          GICAL ACTIVITY RELATIONSHIP/CT
E72           0     2     PHOSPHODIESTERASE-IV/CT

=> e e72
E#   FREQUENCY     AT     TERM
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E73           0     1     PHOSPHODIESTERASE-INHIBITING/CT
E74           0     2     PHOSPHODIESTERASE-INHIBITING MOLECULAR STRUCTURE-BIOLO
                          GICAL ACTIVITY RELATIONSHIP/CT
E75           0     2 --> PHOSPHODIESTERASE-IV/CT
E76           0     2     PHOSPHODIESTERS/CT
E77           3           PHOSPHODOXINS/CT
E78           0     1     PHOSPHOENOLPYRUVATE/CT
E79           0    21     PHOSPHOENOLPYRUVATE CARBOXYKINASE/CT
E80           0    22     PHOSPHOENOLPYRUVATE CARBOXYKINASE (ATP)/CT
E81           0     2     PHOSPHOENOLPYRUVATE CARBOXYKINASE (EC 4.1.1.49)/CT
E82           0    12     PHOSPHOENOLPYRUVATE CARBOXYKINASE (GUANOSINE TRIPHOSPH
                          ATE)/CT
E83           0    13     PHOSPHOENOLPYRUVATE CARBOXYKINASE (PYROPHOSPHATE)/CT
E84           0    15     PHOSPHOENOLPYRUVATE CARBOXYLASE/CT

=> d his

     (FILE 'HOME' ENTERED AT 14:01:42 ON 31 DEC 2009)

     FILE 'CAPLUS' ENTERED AT 14:02:43 ON 31 DEC 2009
                E US2002-060759
                E US2002-060759/AP
L1           1 S E3

     FILE 'ZCAPLUS' ENTERED AT 14:04:32 ON 31 DEC 2009
                SET EXPAND CONTINUOUS
                E  CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE INHIBITOR/C
                E  CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE/CT
                E  PHOSPHODIESTERASE INHIBITOR/CT
                E E46
                E  PHOSPHODIESTERASE IV/CT
                E E72

=> s  9036-21-9
   REGlstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




L3        7908 L2


=> s l3 and (CLL or "chronic lymphocytic leukemia")
          4517 CLL
           106 CLLS
          4542 CLL
                 (CLL OR CLLS)
        276835 "CHRONIC"
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            13 "CHRONICS"
        276841 "CHRONIC"
                 ("CHRONIC" OR "CHRONICS")
         22761 "LYMPHOCYTIC"
        128003 "LEUKEMIA"
          8204 "LEUKEMIAS"
        129581 "LEUKEMIA"
                 ("LEUKEMIA" OR "LEUKEMIAS")
          6974 "CHRONIC LYMPHOCYTIC LEUKEMIA"
                 ("CHRONIC"(W)"LYMPHOCYTIC"(W)"LEUKEMIA")
L4            54 L3 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")

=> s l4 and (ad<19980924 or pd<19980924)
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                 (AD<19980924)
      19260035 PD<19980924
                 (PD<19980924)
L5             3 L4 AND (AD<19980924 OR PD<19980924)

=> d l5 1-3 ibib abs

L5   ANSWER 1 OF 3  ZCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         1998:646421  ZCAPLUS
DOCUMENT NUMBER:          130:261
TITLE:                    Type 4 cyclic adenosine monophosphate
                          phosphodiesterase as a therapeutic target in
                          chronic lymphocytic leukemia
AUTHOR(S):                Kim, Doo Ho; Lerner, Adam
CORPORATE SOURCE:         Department of Medicine, Section of Hematology and
                          Oncology, Boston Medical Center, Boston, MA, 02118,
                          USA
SOURCE:                   Blood (1998), 92(7), 2484-2494
                          CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER:                W. B. Saunders Co.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Theophylline, a drug known to inhibit several classes of adenosine 3'5'
     cyclic monophosphate (cAMP) phosphodiesterases (PDEs), induces apoptosis
     in chronic lymphocytic leukemia (CLL
     ) cells.  Because the PDE target for theophylline in CLL remains
     unknown, the authors examined the ability of isoform-specific PDE inhibitors
     to increase cAMP levels and induce apoptosis in primary CLL
     cells.  Reverse transcriptase-polymerase chain reaction of purified
     CLL cDNA amplified transcripts for PDE1B, 4A and 4B.  The type 4
     PDe inhibitor rolipram but not the type 1 inhibitor vinpocetine increased
     CLL cAMP levels.  Rolipram-inhibitable (type 4) but not
     calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in
     CLL samples.  In samples from 13 of 14 CLL patients,
     rolipram induced apoptosis in a dose-dependent fashion over a 48-h period.
     Interleukin-2 (IL-2)-cultured whole mononuclear cells (WMC) and anti-Ig
     stimulated CD19+ B cells were resistant to the induction of apoptosis by
     rolipram while unstimulated CD19+ B cells, which had a high basal
     apoptotic rate, were more sensitive.  Rolipram stimulated elevations in
     cAMP levels in all four of these cell populations, suggesting that they
     differed in sensitivity to cAMP-induced apoptosis.  Consistent with this
     hypothesis, incubation with the cell permeable cAMP analog dibutyryl-cAMP
     induced apoptosis in CLL cells and unstimulated B cells but not
     in IL-2-cultured WMC or anti-Ig stimulated B cells.  These data identify
     PDE4 as a family of enzymes whose inhibition induces apoptosis in
     CLL cells.
OS.CITING REF COUNT:      50     THERE ARE 50 CAPLUS RECORDS THAT CITE THIS
                                 RECORD (50 CITINGS)
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REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1976:590390 ZCAPLUS
DOCUMENT NUMBER: 85:190390
ORIGINAL REFERENCE NO.: 85:30461a,30464a
TITLE: Cyclic adenosine 3': 5'-monophosphate phosphodiesterase activity in normal and chronic lymphocytic leukemia lymphocytes
AUTHOR(S): Scher, N. S.; Quagliata, F.; Malathi, V. G.; Faig, D.; Melton, R. A.; Silber, R.
CORPORATE SOURCE: Med. Cent., New York Univ., New York, NY, USA
SOURCE: Cancer Research (1976), 36(11, Pt. 1), 3958-62
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sp. activity of cyclic AMP phosphodiesterase (I) was measured in lymphocytes isolated from the blood of normal subjects, from patients with chronic lymphocytic leukemia, and from tonsil tissue. The mean sp. activity of I in the lymphocytes from patients with untreated chronic lymphocytic leukemia was lower than that in lymphocytes from the blood of normal subjects or from tonsils. I levels did not correlate with differences in B- and T-cell lymphocyte subpopulations or with peripheral blood lymphocyte counts.

L5 ANSWER 3 OF 3 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1975:561861 ZCAPLUS
DOCUMENT NUMBER: 83:161861
ORIGINAL REFERENCE NO.: 83:25399a,25402a
TITLE: Adenosine cyclic 3',5'-monophosphate levels and activities of related enzymes in normal and leukemic lymphocytes
AUTHOR(S): Monahan, T. M.; Marchand, N. W.; Fritz, R. R.; Abell, C. W.
CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, USA
SOURCE: Cancer Research (1975), 35(9), 2540-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of cyclic AMP in the regulation of cell division in lymphocytes from healthy donors and patients with chronic lymphocytic leukemia (CLL) was examined by determining the levels of cyclic AMP, glycogen, and the activities of several enzymes closely associated with the metabolism of these cellular components. Intracellular levels of cyclic AMP were measured in normal and CLL lymphocytes in nondividing, dividing, and quiescent (after phytohemagglutinin [PHA] addition states. In normal lymphocytes the levels of cyclic AMP fluctuated throughout the cell cycle after PHA addition, whereas in CLL lymphocytes the levels were .apprx.3-fold lower than in normal cells and remained relatively constant before, during, and after mitogenic stimulation. Normal cells contained .apprx.3-fold lower levels of glycogen than CLL cells, whereas glycogen phosphorylase activities were increased 2- to 4-fold above those in nondividing cells in normal but not in CLL lymphocytes after stimulation with PHA. Furthermore, cyclic AMP phosphodiesterase activities were higher in CLL lymphocytes than in normal ones. Collectively, these studies demonstrated that (1) the intracellular levels of cyclic AMP differed in these 2 cell types; (2) the levels of cyclic AMP and glycogen qual. correlated with activities of enzymes related to these

components; and (3) an inverse relation between the levels of cyclic AMP and cell growth existed in mitogen-stimulated lymphocytes from healthy donors but not from patients with CLL.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

=> d his

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FILE 'CAPLUS' ENTERED AT 14:02:43 ON 31 DEC 2009
E US2002-060759
E US2002-060759/AP
L1 1 S E3

FILE 'ZCAPLUS' ENTERED AT 14:04:32 ON 31 DEC 2009
SET EXPAND CONTINUOUS
E CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE INHIBITOR/C
E CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE/CT
E PHOSPHODIESTERASE INHIBITOR/CT
E E46
E PHOSPHODIESTERASE IV/CT
E E72
S 9036-21-9/REG#

FILE 'REGISTRY' ENTERED AT 14:07:49 ON 31 DEC 2009
L2 1 S 9036-21-9/RN

FILE 'ZCAPLUS' ENTERED AT 14:07:50 ON 31 DEC 2009
L3 7908 S L2
L4 54 S L3 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")
L5 3 S L4 AND (AD<19980924 OR PD<19980924)

=> file registry
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 29.09 35.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -2.46 -2.46

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STRUCTURE FILE UPDATES: 30 DEC 2009 HIGHEST RN 1199751-72-8
DICTIONARY FILE UPDATES: 30 DEC 2009 HIGHEST RN 1199751-72-8

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

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http://www.cas.org/support/stngen/stndoc/properties.html

```
=> s RO 1724
          3994 RO
           995 ROS
          4987 RO
                 (RO OR ROS)
          2728 1724
L6           1 RO 1724
                 (RO(W)1724)

=> d l6

L6   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   77848-04-5  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   RO 1724 (9CI)  (CA INDEX NAME)
MF   Unspecified
CI   MAN
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
               5 REFERENCES IN FILE CA (1907 TO DATE)
               5 REFERENCES IN FILE CAPLUS (1907 TO DATE)


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           995 ROS
          4987 RO
                 (RO OR ROS)
          2728 1724
L7           1 RO-1724
                 (RO(W)1724)

=> d l7

L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   77848-04-5  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   RO 1724 (9CI)  (CA INDEX NAME)
MF   Unspecified
CI   MAN
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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               5 REFERENCES IN FILE CAPLUS (1907 TO DATE)


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FILE COVERS 1907 - 31 Dec 2009 VOL 152 ISS 1
FILE LAST UPDATED: 30 Dec 2009 (20091230/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2009

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=> s l7
L8 5 L7

=> d l8 1-5 ibib abs

L8 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:473224 CAPLUS
DOCUMENT NUMBER: 143:146160
TITLE: Inhibition of mast cell histamine release by specific phosphodiesterase inhibitors
AUTHOR(S): Lau, H. Y. A.; Kam, M. F. A.
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Basic Medical Sciences Building, Chinese University of Hong Kong, Hong Kong, Peop. Rep. China
SOURCE: Inflammation Research (2005), 54(Suppl.), S5-S6
CODEN: INREFB; ISSN: 1023-3830
PUBLISHER: Birkhaeuser Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study characterized the phosphodiesterase (PDE) isoenzyme in rat peritoneal mast cells (RPMC) pharmacol. by comparing the effects of a range of isoenzyme specific inhibitors on anti-IgE induced histamine release. Subsequently, it was investigated whether the simultaneous inhibition of different PDE isoenzymes in mast cells by combinations of isoenzyme specific inhibitors would produce a more complete inhibition of immunol. histamine release. Results suggest that PDE3 and PDE4 are the major isoenzymes regulating IgE-stimulated mediator release from RPMC. The PDE3 inhibitor siguazodan is capable of enhancing the inhibitor actions of the PDE4 inhibitors at concns. (1 μM) where it alone produces no effect. Combinations of a PDE3 inhibitor and a PDE4 inhibitor

reduced histamine release from mast cells more efficaciously than either inhibitor used alone. Such synergistic interaction between inhibitors of these two isoforms of PDE may be the consequence of a more complete inhibition of intracellular PDE enzymes, and will be useful in enhancing the therapeutic efficacy of PDE4 inhibitors in the management of allergic diseases such as asthma.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:531492 CAPLUS
DOCUMENT NUMBER: 119:131492
ORIGINAL REFERENCE NO.: 119:23385a,23388a
TITLE: Comparison of the effect of isobutylmethylxanthine and phosphodiesterase-selective inhibitors on cAMP levels in SH-SY5Y neuroblastoma cells
AUTHOR(S): Morgan, Anthony J.; Murray, Kenneth J.; Challiss, R. A. John
CORPORATE SOURCE: Dep. Pharmacol. Ther., Univ. Leicester, Leicester, LE1 9HN, UK
SOURCE: Biochemical Pharmacology (1993), 45(12), 2373-80
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A comparison of the effects of various phosphodiesterase (PDE) inhibitors upon cellular cAMP levels was undertaken in human neuroblastoma SH-SY5Y cells. When inhibitors such as rolipram and Ro 20 1724 (selective for the low Km cAMP-specific PDE) were used, cAMP levels were seen to rise dramatically under basal (≤60 fold) or forskolin-stimulated (≤200 fold) conditions. However, the non-selective PDE inhibitor isobutylmethylxanthine (IMBX) was 7-18% as effective as these other agents even at 1 mM. The poor efficacy of IBMX was not attributable to concomitant increases in cGMP, to alterations in cAMP egress or to a lack of sensitivity of the cellular PDEs to IBMX inhibition. In additivity expts., IBMX potently and rapidly reduced cAMP that had accumulated after rolipram treatment. The fact that the agonist 2-chloroadenosine can enhance cAMP accumulation in these cells, and that cAMP elevated by rolipram or forskolin can be reduced by adenosine deaminase and theophylline suggest that cell-derived adenosine enhances cAMP in these cells in an autocrine fashion. Since IBMX is an adenosine receptor antagonist, it is suggested that its blockade of endogenous adenosine effects is at least partly responsible for its poor response when compared to other PDE inhibitors which are weaker adenosine receptor antagonists. These results forewarn against assuming that similar levels of cAMP accumulate after application of PDE inhibitors in these cells.
OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1987:98452 CAPLUS
DOCUMENT NUMBER: 106:98452
ORIGINAL REFERENCE NO.: 106:16049a,16052a
TITLE: The insulin- and glucagon-stimulated 'dense-vesicle' high-affinity cyclic AMP phosphodiesterase from rat liver. Purification, characterization and inhibitor sensitivity
AUTHOR(S): Pyne, Nigel J.; Cooper, Michael E.; Houslay, Miles D.
CORPORATE SOURCE: Dep. Biochem., Univ. Glasgow, Glasgow, B12 8QQ, UK
SOURCE: Biochemical Journal (1987), 242(1), 33-42
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hormone-stimulated dense-vesicle cAMP phosphodiesterase was solubilized as a proteolytically clipped species and purified to apparent homogeneity from rat liver with a 2000-3000-fold purification and a 13-18% yield. It appeared to be a dimer (mol. weight (Mr) 112,000), of 2 Mr 57,000 subunits. Solubilization of either a liver or a hepatocyte membrane fraction, with Na cholate in the presence of the protein inhibitor benzamidine, identified 3 protein bands which could be immunopptd. by a polyclonal antibody raised against the pure enzyme. The major band at Mr 62,000 is suggested to be the native dense vesicle enzyme, having a Mr 5000 extension which serves to anchor this enzyme to the membrane and which is cleaved off during proteolytic solubilization; the Mr 200,000 band is an aggregate of the Mr 62,000 species, and the Mr 63,000 species is possibly a precursor. The purified clipped enzyme hydrolyzed cAMP with kinetics indicative of apparent neg. cooperativity, with a Hill coefficient (h) of 0.43 and limiting kinetic consts. of Km1 = 0.3, Km2 = 29 ± 6 μM, Vmax.1 = 0.114, and Vmax.2 = 0.633 unit/mg of protein. It hydrolyzed cGMP with Michaelis kinetics, Km = 10 μM and Vmax = 4.1 munits/mg of protein. Cyclic GMP was a potent inhibitor of cAMP hydrolysis, with concentration giving 50% inhibition of 0.20 μM cGMP when assayed at 0.1 μM cAMP. This enzyme was inhibited potently by several drugs known to exert pos. inotropic effects on the heart, was extremely thermolabile, with a half-life of 4.5 min at 40°, and was shown to be distinct from the rat liver insulin-stimulated, peripheral plasma membrane cAMP phosphodiesterase.

OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1985:469479 CAPLUS

DOCUMENT NUMBER: 103:69479

ORIGINAL REFERENCE NO.: 103:11165a,11168a

TITLE: Modulation of antigenic expression in cultured adult human oligodendrocytes by derivatives of adenosine 3',5'-cyclic monophosphate

AUTHOR(S): Kim, Seung U.; Moretto, Guiseppe; Shin, Doo H.; Lee, Virginia M.

CORPORATE SOURCE: Health Sci. Cent. Hosp., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.

SOURCE: Journal of the Neurological Sciences (1985), 69(1-2), 81-91
CODEN: JNSCAG; ISSN: 0022-510X

DOCUMENT TYPE: Journal

LANGUAGE: English

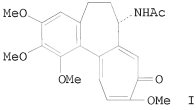
AB Oligodendrocytes were isolated from adult human brains obtained at autopsy by enzyme treatment - Percoll d. gradient centrifugation, and grown in culture. During the 1st week in vitro, these cultures consisted of an enriched population (93-98%) of galactocerebroside-immunoreactive oligodendrocytes. After 2 wk and onward, a larger number of glial fibrillary acidic protein (GFAP)-pos. astrocytes and glial cells doubly pos. for galactocerebroside and GFAP markers was found among the oligodendrocytes. When these cultures were exposed to dibutyryl cyclic AMP, 8-bromocyclic AMP and RO1724, an inhibitor of cyclic nucleotide phosphodiesterase, for 4-14 days, the majority of cells returned to express oligodendrocytic phenotype. These findings suggest the presence of heretofore unidentified transitional or bipotential glial cells in human brains that express both oligodendrocytic and astrocytic phenotypes, and the regulatory role of cAMP derivs. which may induce a stable antigen expression in oligodendrocytes.

L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1981:400278 CAPLUS

DOCUMENT NUMBER: 95:278

ORIGINAL REFERENCE NO.: 95:51a,54a
TITLE: Inhibitors of microtubule assembly potentiate hormone-induced cyclic AMP generation in human leukocytes
AUTHOR(S): Rudolph, Stephen A.; Malawista, Stephen E.
CORPORATE SOURCE: Dep. Pharmacol., Case West. Res. Univ., Cleveland, OH, 44106, USA
SOURCE: Janssen Research Foundation Series (1980), 3(Microtubules Microtubule Inhibitors), 481-95
CODEN: JRFSDU; ISSN: 0165-8352
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Colchicine (I) [64-86-8] and other microtubule assembly inhibitors potentiated the stimulatory effects of phosphodiesterase inhibitors, β-sympathomimetics, prostaglandins, H2-histaminergic agonists, 2-chloroadenosine [146-77-0], and cholera enterotoxin on human leukocyte cyclic AMP [60-92-4] levels. An explanation for the effect of microtubule assembly inhibition on adenylate cyclase activity is that cytoplasmic microtubules limit the mobility of ≥1 membrane components of the hormone-sensitive adenylate cyclase system. When microtubules polymerize in the presence of the inhibitors, these membrane components may interact more frequently with each other to produce active adenylate cyclase complex. If functional synergism between I-like drugs and those hormones whose effects are mediated through cyclic AMP is a more general phenomenon, the appropriate combinations of agents may provide increased therapeutic power in situations in which either class of drugs has proven useful but often not ideal when used alone.

=> file registry
COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 17.00 | 80.05
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CA SUBSCRIBER PRICE | -4.25 | -6.71

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=> s rolipram
L9   11 ROLIPRAM

=> file caplus
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                                                        ENTRY   SESSION
FULL ESTIMATED COST   5.99   86.04

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FILE LAST UPDATED: 30 Dec 2009 (20091230/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2009

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=> s l9
L10   8484 L9

=> s l10 and (CLL or "chronic lymphocytic leukemia")

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           106 CLLS
          4542 CLL
                 (CLL OR CLLS)
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            13 "CHRONICS"
        276841 "CHRONIC"
                 ("CHRONIC" OR "CHRONICS")
         22761 "LYMPHOCYTIC"
        128003 "LEUKEMIA"
          8204 "LEUKEMIAS"
        129581 "LEUKEMIA"
                 ("LEUKEMIA" OR "LEUKEMIAS")
          6974 "CHRONIC LYMPHOCYTIC LEUKEMIA"
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L11          58 L10 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")

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L12           3 L11 AND (AD<19980924 OR PD<19980924)

=> d l12 1-3 ibib abs

L12  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         1998:646421  CAPLUS
DOCUMENT NUMBER:          130:261
TITLE:                    Type 4 cyclic adenosine monophosphate
                          phosphodiesterase as a therapeutic target in
                          chronic lymphocytic leukemia
AUTHOR(S):                Kim, Doo Ho; Lerner, Adam
CORPORATE SOURCE:         Department of Medicine, Section of Hematology and
                          Oncology, Boston Medical Center, Boston, MA, 02118,
                          USA
SOURCE:                   Blood (1998), 92(7), 2484-2494
                          CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER:                W. B. Saunders Co.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Theophylline, a drug known to inhibit several classes of adenosine 3'5'
     cyclic monophosphate (cAMP) phosphodiesterases (PDEs), induces apoptosis
     in chronic lymphocytic leukemia (CLL
     ) cells.  Because the PDE target for theophylline in CLL remains
     unknown, the authors examined the ability of isoform-specific PDE inhibitors
     to increase cAMP levels and induce apoptosis in primary CLL
     cells.  Reverse transcriptase-polymerase chain reaction of purified
     CLL cDNA amplified transcripts for PDE1B, 4A and 4B.  The type 4
     PDe inhibitor rolipram but not the type 1 inhibitor vinpocetine increased
     CLL cAMP levels.  Rolipram-inhibitable (type 4) but not
     calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in
     CLL samples.  In samples from 13 of 14 CLL patients,
     rolipram induced apoptosis in a dose-dependent fashion over a 48-h period.
     Interleukin-2 (IL-2)-cultured whole mononuclear cells (WMC) and anti-Ig
     stimulated CD19+ B cells were resistant to the induction of apoptosis by
     rolipram while unstimulated CD19+ B cells, which had a high basal
     apoptotic rate, were more sensitive.  Rolipram stimulated elevations in
     cAMP levels in all four of these cell populations, suggesting that they
     differed in sensitivity to cAMP-induced apoptosis.  Consistent with this
     hypothesis, incubation with the cell permeable cAMP analog dibutyryl-cAMP
     induced apoptosis in CLL cells and unstimulated B cells but not
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in IL-2-cultured WMC or anti-Ig stimulated B cells. These data identify PDE4 as a family of enzymes whose inhibition induces apoptosis in CLL cells.

OS.CITING REF COUNT: 50 THERE ARE 50 CAPLUS RECORDS THAT CITE THIS RECORD (50 CITINGS)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1976:590390 CAPLUS

DOCUMENT NUMBER: 85:190390

ORIGINAL REFERENCE NO.: 85:30461a,30464a

TITLE: Cyclic adenosine 3': 5'-monophosphate phosphodiesterase activity in normal and chronic lymphocytic leukemia lymphocytes

AUTHOR(S): Scher, N. S.; Quagliata, F.; Malathi, V. G.; Faig, D.; Melton, R. A.; Silber, R.

CORPORATE SOURCE: Med. Cent., New York Univ., New York, NY, USA

SOURCE: Cancer Research (1976), 36(11, Pt. 1), 3958-62
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The sp. activity of cyclic AMP phosphodiesterase (I) was measured in lymphocytes isolated from the blood of normal subjects, from patients with chronic lymphocytic leukemia, and from tonsil tissue. The mean sp. activity of I in the lymphocytes from patients with untreated chronic lymphocytic leukemia was lower than that in lymphocytes from the blood of normal subjects or from tonsils. I levels did not correlate with differences in B- and T-cell lymphocyte subpopulations or with peripheral blood lymphocyte counts.

L12 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1975:561861 CAPLUS

DOCUMENT NUMBER: 83:161861

ORIGINAL REFERENCE NO.: 83:25399a,25402a

TITLE: Adenosine cyclic 3',5'-monophosphate levels and activities of related enzymes in normal and leukemic lymphocytes

AUTHOR(S): Monahan, T. M.; Marchand, N. W.; Fritz, R. R.; Abell, C. W.

CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, USA

SOURCE: Cancer Research (1975), 35(9), 2540-7
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The role of cyclic AMP in the regulation of cell division in lymphocytes from healthy donors and patients with chronic lymphocytic leukemia (CLL) was examined by determining the levels of cyclic AMP, glycogen, and the activities of several enzymes closely associated with the metabolism of these cellular components. Intracellular levels of cyclic AMP were measured in normal and CLL lymphocytes in nondividing, dividing, and quiescent (after phytohemagglutinin [PHA] addition states. In normal lymphocytes the levels of cyclic AMP fluctuated throughout the cell cycle after PHA addition, whereas in CLL lymphocytes the levels were .apprx.3-fold lower than in normal cells and remained relatively constant before, during, and after mitogenic stimulation. Normal cells contained .apprx.3-fold lower levels of glycogen than CLL cells, whereas glycogen phosphorylase activities were increased 2- to 4-fold above those in nondividing cells in normal but not in CLL lymphocytes after

stimulation with PHA. Furthermore, cyclic AMP phosphodiesterase activities were higher in CLL lymphocytes than in normal ones. Collectively, these studies demonstrated that (1) the intracellular levels of cyclic AMP differed in these 2 cell types; (2) the levels of cyclic AMP and glycogen qual. correlated with activities of enzymes related to these components; and (3) an inverse relation between the levels of cyclic AMP and cell growth existed in mitogen-stimulated lymphocytes from healthy donors but not from patients with CLL.
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

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L1 1 S E3

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E PHOSPHODIESTERASE IV/CT
E E72
S 9036-21-9/REG#

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L2 1 S 9036-21-9/RN

FILE 'ZCAPLUS' ENTERED AT 14:07:50 ON 31 DEC 2009
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L4 54 S L3 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")
L5 3 S L4 AND (AD<19980924 OR PD<19980924)

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L7 1 S RO-1724

FILE 'CAPLUS' ENTERED AT 14:11:25 ON 31 DEC 2009
L8 5 S L7

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L9             11 S ROLIPRAM

     FILE 'CAPLUS' ENTERED AT 14:13:11 ON 31 DEC 2009
L10         8484 S L9
L11           58 S L10 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")
L12            3 S L11 AND (AD<19980924 OR PD<19980924)

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L13          SEL L9 1- CHEM :     107 TERMS

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FULL ESTIMATED COST                                    15.09     130.50

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CA SUBSCRIBER PRICE                                     0.00      -9.26

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SEARCH OF L13 IS APPROXIMATELY 68% COMPLETE
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L17          8 DUP REM L16 (3 DUPLICATES REMOVED)

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L17  ANSWER 1 OF 8     MEDLINE on STN
ACCESSION NUMBER:   1998421394     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9746789
TITLE:              Type 4 cyclic adenosine
                    monophosphate phosphodiesterase as a
                    therapeutic target in chronic lymphocytic
                    leukemia.
AUTHOR:             Kim D H; Lerner A
CORPORATE SOURCE:   Department of Medicine, Section of Hematology and Oncology,
                    Boston Medical Center, Boston, MA 02118, USA.
SOURCE:             Blood, (1998 Oct 1) Vol. 92, No. 7, pp. 2484-94.
                    Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        199810
ENTRY DATE:         Entered STN: 29 Oct 1998
                    Last Updated on STN: 3 Mar 2000
                    Entered Medline: 19 Oct 1998
AB   Theophylline, a drug known to inhibit several classes of adenosine 3'5'
     cyclic monophosphate (cAMP) phosphodiesterases (PDEs),
     induces apoptosis in chronic lymphocytic
     leukemia (CLL) cells.  Because the PDE target for
     theophylline in CLL remains unknown, we examined the ability of
     isoform-specific PDE inhibitors to increase cAMP levels and induce
     apoptosis in primary CLL cells.  Reverse
     transcriptase-polymerase chain reaction of purified CLL cDNA
     amplified transcripts for PDE1B, 4A and 4B.  The type 4 PDE inhibitor
     rolipram but not the type 1 inhibitor vinpocetine increased
     CLL cAMP levels.  Rolipram-inhibitable (type 4) but not
     calcium-calmodulin augmented (type 1) PDE enzyme activity was detected in
     CLL samples.  In samples from 13 of 14 CLL patients,
     rolipram induced apoptosis in a dose-dependent fashion over a
     48-hour period.  Interleukin-2 (IL-2)-cultured whole mononuclear cells
     (WMC) and anti-Ig stimulated CD19(+) B cells were resistant to the
     induction of apoptosis by rolipram while unstimulated CD19(+) B
     cells, which had a high basal apoptotic rate, were more sensitive.
     Rolipram stimulated elevations in cAMP levels in all four of these
     cell populations, suggesting that they differed in sensitivity to
     cAMP-induced apoptosis.  Consistent with this hypothesis, incubation with
     the cell permeable cAMP analog dibutyryl-cAMP induced apoptosis in
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CLL cells and unstimulated B cells but not in IL-2-cultured WMC or anti-Ig stimulated B cells. These data identify PDE4 as a family of enzymes whose inhibition induces apoptosis in CLL cells.

L17 ANSWER 2 OF 8 MEDLINE on STN
ACCESSION NUMBER: 1985266339 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2991669
TITLE: Phorbol ester-induced loss of colchicine ultrasensitivity in chronic lymphocytic leukaemia lymphocytes.
AUTHOR: O'Connor T W
SOURCE: Leukemia research, (1985) Vol. 9, No. 7, pp. 885-95.
Journal code: 7706787. ISSN: 0145-2126.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198509
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 3 Sep 1985

AB On exposure to the phorbol ester 12-O-tetradecanoyl-13-acetate (TPA) the pathological (non-dividing) lymphocytes of B-cell chronic lymphocytic leukaemia (CLL) lose their characteristic ultrasensitivity to the cytocidal action of colchicine in vitro. They are no longer killed in 1 day by the drug at 10(-6)M-concentration. The effect was the same whether the cells were incubated in the continuous presence of TPA, or subjected instead to pulse-treatment with it (for as little as 5 min.). Colchicine at one thousand times greater concentration was now needed to kill the cells. CLL lymphocytes already primed to undergo interphase death by pretreatment with colchicine could be prevented from doing so by early addition of TPA. A marked proportion of those CLL lymphocytes destined to undergo early spontaneous death in vitro in the absence of colchicine could be prevented from doing so by TPA. The loss of colchicine ultrasensitivity applied to cells which had not yet undergone TPA-induced morphological transformation to blast-like cells or differentiation to cells containing abundant cytoplasmic immunoglobulins (CIg). These transformed cells materialised in greatest incidence (70-80%) after 3 days of culture, an observation in agreement with others workers.

L17 ANSWER 3 OF 8 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1986078709 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3000540
TITLE: [Phosphatidylethanolamine methylase and cyclic nucleotide phosphodiesterase activities in human B lymphoid hemopathies].
Etude des activites phosphatidylethanolamine methylase et nucleotides cycliques phosphodiesterases dans les hemopathies lymphoides B humaines.
AUTHOR: Pacheco Y; Magaud J P; Dubois M; French M; Fonlupt P; Prigent A F; Rey C; Germain D; Pacheco H
SOURCE: Comptes rendus de l'Academie des sciences. Serie III, Sciences de la vie, (1985) Vol. 301, No. 16, pp. 711-6.
Journal code: 8503078. ISSN: 0764-4469.
PUB. COUNTRY: France
DOCUMENT TYPE: (COMPARATIVE STUDY)
(ENGLISH ABSTRACT)

Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198602
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 30 Oct 2002
Entered Medline: 20 Feb 1986
AB Phospholipid methylase and cyclic nucleotide phosphodiesterase activities were studied in human B lymphoid hemopathies (51 patients: acute lymphoblastic leukemia, B lymphoma, chronic lymphocytic leukemia, hairy cell leukemia) and compared with activities in lymphoblastid and Burkitt lymphoma cell lines and with normal B lymphocytes: methylase activity proved to be lower in ALL and high grade lymphoma and inversely related to the percent of cells in S phase state; the A/G ratio of phosphodiesterases was low in ALL and CLL and high in hairy cell leukemia and it was related to the percent of cells in S phase state.

L17 ANSWER 4 OF 8 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1978187356 EMBASE
TITLE: Catecholamine hormone receptors are reduced on chronic lymphocytic leukaemic lymphocytes.
AUTHOR: Sheppard, J.R.; Gormus, R.; Moldow, C.F.
CORPORATE SOURCE: Dept. Genet. Cell Biol., Dight Inst. Hum. Genet., Minneapolis, Minn., United States.
SOURCE: Nature, (1977) Vol. 269, No. 5630, pp. 693-695.
ISSN: 0028-0836 CODEN: NATUAS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
AB Comparison of circulating lymphocytes from chronic lymphocytic leukemia (CLL) patients with those from normal human controls indicates that cyclic AMP levels, cyclic nucleotide phosphodiesterase and adenylate cyclase activities are changed in the CLL lymphocyte. The membrane enzyme activity of 5' nucleotidase as well as complement, antigen and lectin binding are also altered in the CLL plasma membrane. The observation that catecholamine hormone (β-adrenergic) responsiveness is depressed in CLL lymphocytes is further evidence for a functionally altered plasma membrane. It is then shown that the number of β-adrenergic hormone receptor sites is reduced on CLL lymphocyte membranes while the catalytic capacity of the cyclase enzyme is normal. The low density of catecholamine hormone receptors could account for the altered cyclic AMP metabolism and may contribute to the unregulated growth of CLL lymphocytes.

L17 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1977023691 MEDLINE
DOCUMENT NUMBER: PubMed ID: 184920
TITLE: Cyclic adenosine 3':5'-monophosphate phosphodiesterase activity in normal and chronic lymphocytic leukemia lymphocytes.
AUTHOR: Scher N S; Quagliata F; Malathi V G; Faig D; Melton R A; Silber R
SOURCE: Cancer research, (1976 Nov) Vol. 36, No. 11 Pt 1,

pp. 3958-62.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197612
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 30 Dec 1976
AB The specific activity of cyclic adenosine 3':5'-monophosphate phosphodiesterase was measured in lymphocytes isolated from the blood of normal subjects, from patients with chronic lymphocytic leukemia, and from tonsil tissue. The mean specific activity of cyclic adenosine 3':5'-monophosphate phosphodiesterase in the lymphocytes from patients with untreated chronic lymphocytic leukemia was lower than that in lymphocytes from the blood of normal subjects or from tonsils. Cyclic adenosine 3':5'-monophosphate phosphodiesterase levels did not correlate with differences in B- and T-cell lymphocyte subpopulations or with peripheral blood lymphocyte counts.

L17 ANSWER 6 OF 8 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1977190776 EMBASE
TITLE: Cyclic adenosine 3':5' monophosphate phosphodiesterase activity in normal and chronic lymphocytic leukemia lymphocytes.
AUTHOR: Scher, N.S.; Quagliata, F.; Malathi, V.G.; et. al.
CORPORATE SOURCE: Dept. Med., New York Univ. Med. Cent., New York, N.Y. 10016, United States.
SOURCE: Cancer Research, (1976) Vol. 36, No. 11, pp. I.
ISSN: 0008-5472 CODEN: CNREA8
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
029 Clinical and Experimental Biochemistry
LANGUAGE: English
AB The specific activity of cyclic adenosine 3':5' monophosphate phosphodiesterase was measured in lymphocytes isolated from the blood of normal subjects, from patients with chronic lymphocytic leukemia, and from tonsil tissue. The mean specific activity of cyclic adenosine 3':5' monophosphate phosphodiesterase in the lymphocytes from patients with untreated chronic lymphocytic leukemia was lower than that in lymphocytes from the blood of normal subjects or from tonsils. Cyclic adenosine 3':5' monophosphate phosphodiesterase levels did not correlate with differences in B and T cell lymphocyte subpopulations or with peripheral blood lymphocyte counts.

L17 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1975207267 MEDLINE
DOCUMENT NUMBER: PubMed ID: 167962
TITLE: Cyclic adenosine 3':5'-monophosphate levels and activities

of related enzymes in normal and leukemic lymphocytes.
AUTHOR: Monahan T M; Marchand N W; Fritz R R; Abell C W
SOURCE: Cancer research, (1975 Sep) Vol. 35, No. 9, pp. 2540-7.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197511
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 8 Nov 1975

AB The role of cyclic adenosine 3':5'-monophosphate (cyclic 3':5'-AMP) in the regulation of cell division in lymphocytes obtained from healthy donors and from patients with chronic lymphocytic leukemia (CLL) was investigated by determining the levels of cyclic 3':5'-AMP and glycogen and also the activities of several enzymes that are closely associated with the metabolism of these cellular components. Intracellular levels of cyclic 3':5'-AMP were measured in normal and CLL lymphocytes in nondividing, dividing, and quiescent [after phytohemagglutinin (PHA) addition]states. In normal lymphocytes the levels of cyclic 3':5'-AMP fluctuated throughout the cell cycle after PHA addition, whereas in CLL lymphocytes the levels were approximately 3-fold lower than in normal cells and remained relatively constant before, during, and after mitogenic stimulation. Normal cells contained approximately 3-fold lower levels of glycogen than CLL cells, whereas glycogen phosphorylase activities were increased 2- to 4-fold above those in nondividing cells in normal but not in CLL lymphocytes after stimulation with PHA. Furthermore, cyclic 3':5'-AMP phosphodiesterase activities were higher in CLL lymphocytes than in normal ones. Collectively, these studies demonstrated that (a) the intracellular levels of cyclic 3':5'-AMP differ in these two cell types; (b) the levels of cyclic 3':5'-AMP and glycogen qualitatively correlate with the activities of the enzymes that are related to these components; and (c) an inverse relationship between the levels of cyclic 3':5'-AMP and cell growth exists in mitogen-stimulated lymphocytes from healthy donors but not from patients with CLL. These biochemical differences are presumed to exist between normal and "leukemic" lymphocytes, but alternatively they may reflect normal populations of immunologically distinct lymphocytes.

L17 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1975:35147 BIOSIS
DOCUMENT NUMBER: PREV197511035147; BR11:35147
TITLE: STUDIES ON THE MEMBRANES OF HUMAN NORMAL AND LEUKEMIC LYMPHOCYTES.
AUTHOR(S): ABELL C W; FRITZ R R; NOVAK R A; MONAHAN T M
SOURCE: (1974) pp. 227-251. SCHULTZ, JULIUS AND RONALD E. BLOCK (ED.). MIAMI WINTER SYMPOSIA, VOL. 8. MEMBRANE TRANSFORMATIONS IN NEOPLASIA. MIAMI, FLA., U.S.A., JAN. 17-18, 1974. XV+297P. ILLUS. ACADEMIC PRESS: NEW YORK, N.Y., U.S.A; LONDON, ENGLAND. ISBN 0-12-632760-2.
DOCUMENT TYPE: Book
FILE SEGMENT: BR
LANGUAGE: Unavailable

=> d his

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     (FILE 'HOME' ENTERED AT 14:01:42 ON 31 DEC 2009)

     FILE 'CAPLUS' ENTERED AT 14:02:43 ON 31 DEC 2009
                E US2002-060759
                E US2002-060759/AP
L1            1 S E3

     FILE 'ZCAPLUS' ENTERED AT 14:04:32 ON 31 DEC 2009
                SET EXPAND CONTINUOUS
                E  CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE INHIBITOR/C
                E  CYCLIC ADENOSINE MONOPHOSPHATE PHOSPHODIESTERASE/CT
                E  PHOSPHODIESTERASE INHIBITOR/CT
                E E46
                E  PHOSPHODIESTERASE IV/CT
                E E72
                S 9036-21-9/REG#

     FILE 'REGISTRY' ENTERED AT 14:07:49 ON 31 DEC 2009
L2            1 S 9036-21-9/RN

     FILE 'ZCAPLUS' ENTERED AT 14:07:50 ON 31 DEC 2009
L3         7908 S L2
L4           54 S L3 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")
L5            3 S L4 AND (AD<19980924 OR PD<19980924)

     FILE 'REGISTRY' ENTERED AT 14:10:25 ON 31 DEC 2009
L6            1 S RO 1724
L7            1 S RO-1724

     FILE 'CAPLUS' ENTERED AT 14:11:25 ON 31 DEC 2009
L8            5 S L7

     FILE 'REGISTRY' ENTERED AT 14:13:02 ON 31 DEC 2009
L9           11 S ROLIPRAM

     FILE 'CAPLUS' ENTERED AT 14:13:11 ON 31 DEC 2009
L10        8484 S L9
L11          58 S L10 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")
L12           3 S L11 AND (AD<19980924 OR PD<19980924)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:16:34 ON 31 DEC 2009

     FILE 'REGISTRY' ENTERED AT 14:16:42 ON 31 DEC 2009
                SET SMARTSELECT ON
L13          SEL L9 1- CHEM :     107 TERMS
                SET SMARTSELECT OFF

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:16:44 ON 31 DEC 2009
L14        31250 S L13
L15           72 S L14 AND (CLL OR "CHRONIC LYMPHOCYTIC LEUKEMIA")
L16           11 S L15 AND (AD<19980924 OR PD<19980924)
L17            8 DUP REM L16 (3 DUPLICATES REMOVED)

=>

---Logging off of STN---


=>
Executing the logoff script...
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=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	19.26	149.76

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.26

STN INTERNATIONAL LOGOFF AT 14:21:51 ON 31 DEC 2009